Vinyl Amide Reactions in the Presence of Gold(I) Catalyst

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Declaration

I hereby declare that the work presented in this thesis has been conducted independently and in accordance with the rules and regulations for the integrated Master’s degree in Industrial chemistry and biotechnology (sivilingeniør/masters programme, 5 years) at the Norwegian University of Science and Technology (NTNU). The work has been conducted from October 2011 to March 2012.

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Summary

The purpose of this project has been to investigate reactions with vinyl amides in the presence of gold(I) catalyst. Vinyl amides are good nucleophiles, and four vinyl amides were synthesized in a copper catalyzed cross-coupling reaction (Scheme 1). Reactions of 6a-b, 10 and 12 afforded acyclic vinyl amides 4a-b (33-43%) and heterocyclic vinyl amides N-vinyl valerolactam 9 (43%) and 3-vinyloxazolidin-2-one 11 (89%).

Terminal triple bond systems are useful in gold(I) catalyzed reactions since gold(I) activates the π-cloud for nucleophilic attack. Propargyl acetals are suitable substrates for such gold(I) catalyzed reactions. Thus, two new propargyl acetals, methoxy acetal 1a and ethoxy acetal 1b, were synthesized from alcohol 2 and vinyl ethers 3a-b in acid catalyzed reactions (40-60% yields) (Scheme 2).

The first part of this project has been to investigate gold(I) catalyzed reactions of propargyl acetals with vinyl amides. Gold catalysts are known to be alkynophilic, activating π-systems such as propargylic substrates for nucleophilic attack, by e.g vinyl amides. This makes propargyl acetals 1a-b and the vinyl amides suitable substrates in gold(I) catalyzed reactions.
Gold catalyst I has been used in this project (Figure 1).

The cyclopentenyl products 17a and 18a (22-51%) were obtained in a gold(I) catalyzed [3+2] cycloaddition reaction of methoxy acetal 1a and vinyl amides 9 and 11, as two vinyl ether isomers. The corresponding products 17b and 18b (14-36%) were obtained in a similar reaction (Scheme 3).

Formation of the cyclopentenyl products 17-18 indicates that electron releasing substrates would rather undergo cyclopentenylation than cyclopropanation.

The second part of this project was the investigation of vinyl amide dimerization reactions. A variety of catalytic conditions are known to promote selective homo-and heterodimerization of vinyl compounds. We wanted to investigate dimerization reactions of acyclic vinyl amides 4a-b and the heterocyclic vinyl amides 9 and 11 in the presence of phenylacetylene and gold(I) catalyst. The vinyl amides 4b, 9 and 11 successfully afforded homodimerization products 23, 25 and 26 in 63-77% yield (Scheme 4).

The effect of the gold(I) catalyst in the new dimerization reactions is discussed in this project.
Sammendrag

Hovedmålet med denne masteroppgaven har vært å utforske reaksjoner med vinyl amider i nærvær av gull(I)katalysator. Vinylamider er gode nukleofiler i gullkatalyserte reaksjoner, og fire vinyl amider ble syntetisert i kobberkatalyserte cross-koblingsreaksjoner (Skjema 1). Asykliske vinylamider 4a-b (33%), og heterosykliske vinylamider N-vinylvalerolactam 9 (43%) og 3-vinyloxazolidin-2-one 11 (89%) ble syntetisert fra vinylbromid og hhv 6a-b, δ-valerolactam 10 og oxazolidin-2-one 12.

Terminale trippelbond-systemer er nyttige i gull(I)katalyserte reaksjoner. Gull(I) er kjent for å aktivere π-systemer for nukleofilt angrep. To nye propargylacetaler, metoksyacetal 1a og etoksyacetal 1b, ble derfor fremstilt i en syrekatalysert reaksjon (40-60% utbytte) (Skjema 2).

Første del av dette prosjektet har vært å undersøke gull(I)katalyserte reaksjoner av propargylacetaler med vinylamider. Gull(I)katalysatorer er alkynofile, og aktiverer π-systemer som f.eks propargylsubstrater for nukleofilt angrep fra f.eks vinylamider. Dette gjør propargylacetaler 1a-b og vinylamider 4a-b, 9 og 11 til egne substrater i gull(I)katalyserte reaksjoner.
I dette prosjektet har gullkatalysator I blitt benyttet (Figur 1).

![Gullkatalysator I](image)

Figur 1 Gull(I)katalysator benyttet i prosjektet

Syklopentenylprodutene 17a og 18a (22-51%) ble fremstilt i en gull(I)katalysert [3+2] sykloaddisjonsreaksjon fra metoksylacetal 1a og vinylamid 9. Produktene ble isolert som to isomere vinyleter. I en korresponderende reaksjon ble syklopentenylprodukter 17b og 18b (14-36%) fremstilt (Skjema 3).

![Skjema 3](image)

Skjema 3 Gull(I)katalysert reaksjon med acetal 1a og heterosyklisk vinylamider 9 og 11

Dannelsen av produkt 17-18 indikerer at [3+2] sykloaddisjon er foretrukket fremfor syklopropanering dersom man har en gull(I)katalysert reaksjon med et elektroniltrekkende substrat, slik som propargylacetaler, og elektronodonerende substrat, slik som vinylamider.

Andre del av dette prosjektet har vært å undersøke dimeriseringsreaksjoner av vinylamider. Ulike katalytiske betingelser er kjent for å gi selektiv homo- og heterodimerisering av vinylforbindelser. Vi ønsket å undersøke dimerisering av asykliske vinylamider (4a-b) og heterosykliske vinylamider (9 og 11) i reaksjoner med fenylacetylen og gull(I)katalysator. Dimeriseringsprodukter 23, 25 og 26 ble fremstilt fra hhv vinylamider 4b, 9 og 11 (72-85% utbytte) (Skjema 4).

![Skjema 4](image)

Skjema 4 Dimeriseringsreaksjoner av vinylamider 4b, 9 og 11

Effekten av gull(I)katalysatoren i disse nye dimeriseringsreaksjoner er diskutert i dette prosjektet.

VIII
Abbreviations

Ac     Acetal
arom   aromatic
br     broadened
calc   calculated
CDCl$_3$  deuterated chloroform
cm$^{-1}$ wave number, reciprocal centimeter
cnc    concentrated
COSY  Correlated Spectroscopy
$\delta$ chemical shift [ppm]
d     doublet (NMR)
D$_2$O  deuterated water
DCM    Dichloromethane
dd     doublet of doublet (NMR)
ddt    doublet of doublet of triplet (NMR)
dt     doublet of triplet (NMR)
dm     doublet of multiplet (NMR)
DMF    Dimethylformamide
DMSO   Dimethyl sulfoxide
EE     1-Ethoxyl-Ethyl ether
e.g.   exempli gratia (for example)
EI     Electron Impact (MS)
equiv  equivalent
ERG    Electron Releasing Groups
ESI    Electron Spray Impact (MS)
Et Ethyl

*et al.* *et alia* (and others)

EWG Electron Withdrawing Groups

GC Gas Chromatography

h hour

HMBC Heteronuclear Multi Bond Coherence

HR High Resolution (MS)

HSQC Heteronuclear Single Quantum Coherence

Hz Hertz

IR Infrared spectroscopy

\( J \) coupling constant \([\text{Hz}]\)

L Ligand

\( m \) multiplet (NMR)

M Molar \([\text{mol/litre}]\)

Me Methyl

MeOH Methanol

mg milligram

MHz MegaHertz

\( \mu \text{mol} \) micromol

min minutes

\( \text{mL} \) millilitres

\( \text{mmol} \) millimol

MOP 2-MethOxy-2-Propyl ethers

mp melting point

MS Mass spectroscopy

NHC N-Heterocyclic Carbene

nm nanometer

NMR Nuclear Magnetic Resonance spectroscopy

NOESY Nuclear Overhauser Effect spectroscopy

Nu Nucleophile

obsd observed

X
\pi \quad \text{pi}

Ph \quad \text{Phenyl}

obsd \quad \text{observed}

Piv \quad \text{Trimethyl acetyl}

ppm \quad \text{parts per million}

PPTS \quad \text{para-Toluene Sulfonic acid}

quin \quad \text{quintett (NMR)}

R_f \quad \text{Retention factor (TLC)}

rt \quad \text{room temperature}

\sigma \quad \text{sigma}

s \quad \text{singlet (NMR)}

t \quad \text{triplet (NMR)}

t-Bu \quad \text{tert-Butyl}

TFA \quad \text{Trifluoro acetic acid}

THF \quad \text{Tetrahydrofuran}

THP \quad \text{Tetrahydropyranyl ether}

TLC \quad \text{Thin Layer Chromatography}

TMS \quad \text{Trimethylsilyl}

Ts \quad \text{Tosyl}

UV \quad \text{Ultraviolet}

Å \quad \text{Ångstrom}
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Chapter 1

Introduction

It is well known that gold(I) complexes are versatile and efficient catalysts to promote a variety of organic transformations. In particular, gold(I) catalysts have an exceptional ability to activate C-C multiple bonds towards nucleophilic attack. They have an affinity towards $\pi$-systems, such as triple bond systems. This makes gold catalysts useful in reactions with propargyl esters and propargyl acetals.

1.1 Aim of project

In a recent study of cyclopropanation by Fiksdahl et al, $[3+2]$ cycloadditions of propargyl esters and vinyl amides have been observed. This master project is a continuation of the previous project carried out by Jørn E. Tungen and Christian Sperger in the group of prof. Anne Fiksdahl. Their aim was to study the cyclopropanation pathway in reactions involving propargyl esters and vinyl compounds in the presence of gold(I) catalyst. They discovered that $[3+2]$ cycloaddition took place for some compounds. The main goal for the present project was to study gold(I) catalyzed $[3+2]$ cycloaddition of propargyl acetals 1 and vinyl amides 4, 9 and 11 (Figure 1.1).

However, during these studies, a homodimerization of some vinyl amides occurred. Thus, a second aim was to study dimerization reactions involving gold(I) catalyst, phenylacetylene and different vinyl amides. Homodimerization was investigated, but some studies on heterodimerization between cyclic and acyclic vinyl amides were also included.
Chapter 2

Theory

2.1 General principles of organometallic chemistry

Gold(I) catalyzed reactions and reactions with other organometallic compounds is a field in organometallic chemistry that is less explored. Organometallic compounds are in general both air- and moisture sensitive, and this has made chemists careful to use organometallic chemistry in their syntheses. Well known compounds such as alkyl lithiums or Grignard reagents are known to hydrolyze vigorously in solution, and organoaluminiums even react with air.

Organometallic compounds are compounds containing at least one metal-carbon bond. The presence of electrons in the $d$-orbitals separates the transition metals from the main group metals. The transition metals have free $d$-orbitals and are also called d-block metals. The $d$-orbitals are filled for the transition metals as we move to the right in the Periodic Table. But as these orbitals often are lower in energy than the next $s$- or $p$-orbital, the transition metals have filled $d$-orbitals with free $s$- and $p$-orbitals. This enables transition metal ions to bind to ligands ($L$) and form complexes of type $ML_n$. Metal-carbon bond of elements to the right in the Periodic Table are of a more covalent character than of those to the left. This makes compounds such as alkyl lithium, Grignard reagents, and alkyl aluminiums reactive towards hydrolysis, while organosilicon compounds are more stable.

If a complex obey the 18-electron rule for a stable metal complex, the centre metal atom has noble gas configuration of 18 electrons in the valence shells.

Transition metals can have a number of ligands attached to them and each ligand can be attached with more than one site. Unlike the transition metals, the ligands usually have full sp$^3$-hybridized orbitals that can overlap with the empty 'dsp' orbital of the metal, thus leading to an increase in electron density on the central metal atom. As for Grignard reagents, R-Mg, the ligands are attached to the metal through $\sigma$-bonds, as $\sigma$-complexes, as seen in Figure 2.1. R$_3$P, R$_3$N and H$^-$ are examples of such $\sigma$-donors.

![Figure 2.1 σ-bond between vacant 'dps' orbital of metal and filled lone pair on ligand](image)

Figure 2.1 σ-bond between vacant 'dps' orbital of metal and filled lone pair on ligand
A $\sigma$-bond interaction is also possible with any filled $d$ orbital of the metal and vacant ligand orbital with appropriate symmetry such as $\pi^*$ orbitals, as shown in Figure 2.2. This decrease in electron density on the central metal atom is called back-bonding.\cite{6} An example of this type of bond is a complex with CO as a ligand.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure2_2.png}
\caption{2.2 a) Filled d orbital, empty $\pi^*$ b) Empty d orbital, filled sp}
\end{figure}

In alkene bonding there are no $\sigma$-bonds to the metal. The metal-alkene bond is located in the middle of the $\pi$-bond in between two $p$-orbitals. These types of complexes are called $\pi$-complexes and the metal-ligand bond has both $\sigma$- and $\pi$ character, as shown in Figure 2.3.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure2_3.png}
\caption{2.3 a) Vacant d orbital, filled $\pi$ on ligand b) Filled d orbital, empty olefin acting as $\sigma$-donor $\pi^*$ orbitals}
\end{figure}

The stereoselectivity of these reactions is usually trans, as the incoming reagents usually approach from the side opposite of the metal.\cite{6}

### 2.2 Gold catalysis

Gold catalysis has been neglected by organic chemists for a long time. However, homogenous gold catalysis of organic reactions have expanded rapidly in recent years.\cite{7} Gold can exist in two oxidation states; Au(I) and Au(III).\cite{2} Although Au complexes can undergo oxidative addition/reductive elimination, these are rare. The lack of change in oxidation state makes coupling chemistry difficult.\cite{2} Unlike alkyl lithium, Grignard and organoaluminium mentioned earlier, gold catalysts are not sensitive to air or moisture due to their high oxidation potential.\cite{8} Gold complexes are less oxophilic than common Lewis acids, but slightly more reactive as 'soft' carbon Lewis acids (e.g double and triple bonds).\cite{2} This allows reactions to take place in the presence of oxygen, water and alcohols.\cite{9} In addition, gold catalysts show high tolerance towards different functional groups, thus it is possible to avoid protecting groups. In this way gold catalysts are more effective towards 'step-economy'.\cite{10} The mentioned properties of the gold complexes makes them useful in organic synthesis, where it is possible to reach complex molecules in a few reaction steps.\cite{10}
There are many commercially available gold(I) catalysts, as shown in Figure 2.4. Typical ligands are tertiary phosphine ligands (I-III).\textsuperscript{[11]} Other ligands such as NHC is also used (IV).

In our studies, we have used catalyst I. This is a cationic catalyst, which activates \( \pi \)-systems, including alkenes, alkynes and allenes.\textsuperscript{[12]}

In case of reactions with alkynes, the catalyst activates the triple bond for nucleophilic attack in a catalytic cycle, shown in Scheme 2.1.
The gold catalyst activates the triple bond, which is then attacked by a nucleophile in an anti fashion. Gold is further replaced by a proton through protodeauration to obtain the alkene and regenerate the catalyst.

By varying the nature of the nucleophile, many different complex structures can be obtained. The incorporation of an internal nucleophile in 1,6-diyne substrates (V) has enabled tandem cyclization. This method has previously been developed in the Fiksdahl research group, where a number of new bicyclic heterocycles (VI-X) were formed.\cite{9}

\[ R \text{NuH} \]

\[ \text{Au}(L)\text{Cl} \]

\[ \text{Au-salt} \]

\[ \text{Ag-salt} \]

\[ \text{X:NTs} \]

\[ \text{X:O} \]

\[ \text{X:NR}^1 \]

\[ \text{NuH: NH}_2, \text{CO}_2 \text{H}, \text{CONHR}, \text{NHTs} \]

Scheme 2.2 Gold(I) catalyzed tandem cyclizations

### 2.3 Gold(I) catalyzed [3+2] cycloaddition of propargyl substrates with vinylamides

A number of cyclization and cycloaddition reactions have been shown to take place in the presence of Au(I) catalysts, mainly with phosphine ligands.\cite{11} In our research group, [1+2] cycloaddition of propargyl esters have been studied previously.\cite{3} The proposed pathway involves an attack of the acyl group on the inner carbon of the activated triple bond. This is known as 1,2-acyloxy shift.\cite{8} The intermediate, a gold carbenoid, acts as a carbene to give [1+2] cycloaddition with a double bond and gives a cyclopropane-product. During these studies, it was discovered that some compounds, in particular propargyl acetals, would rather undergo [3+2] cycloaddition, giving a cyclopentenyl product.\cite{3} The proposed reaction pathways for the [1+2] and [3+2] cycloaddition of propargyl substrates are shown in Scheme 2.3.

\[ \text{XI-XV: R=COR'} \]

\[ \text{XI': R=CR''OR'''} \]

\[ \text{XII'-XV': R=OR'''} \]

\[ \text{R}_3 \]

\[ \text{OR} \]

\[ \text{R}_2 \]

\[ \text{H} \]

\[ \text{R}_5 \]

\[ \text{XIIIb', XIIIb'} \]

\[ \text{XIIIa, XIIIa'} \]

\[ \text{XIIa}, \text{XIIIa'} \]

\[ \text{XII, XIII', XIV', XV', XV'} \]

\[ \text{[1+2]/[3+2] cycloadditions} \]

Scheme 2.3 Gold promoted activation of propargylic substrates
The mechanism proposes an equilibrium between the gold carbenoid and the allylic cation. Fiks-dahl et al recently investigated propargylic esters (XI) as precursors for the formation of gold carbenoids (XIII). These carbenoids are proposed to be reactive intermediates in a variety of reactions, olefin cyclopropanations in particular.\textsuperscript{[13][14][15]}

Propargyl acetals (XI') are also known to undergo rearrangement to provide gold carbenoids.\textsuperscript{[16]} The reaction is a modified 1,2-/1,4-alkoxy shift method, including cleavage of a ketone or an aldehyde leaving group (Scheme 2.4). Such reactions may involve an active gold species with a more delocalized positive charge, represented as XIIIb' in Scheme 2.3.\textsuperscript{[17]}

![Scheme 2.4 Gold(I) catalyzed [3+2] cycloaddition of propargyl acetals with vinyl derivatives](image)

### 2.4 Dimerization of vinylamides

In contrast to the reductive coupling products obtained by certain transition metal catalyzed tail-to-tail dimerization of alkenes, homodimerization may take place by a head-to-tail or head-to-head coupling (Scheme 2.5).\textsuperscript{[18]}

A variety of catalytic conditions, based on e.g. Lewis acids; In, Pd, Fe, Ni, Ru, Co and Rh complexes are known to promote selective head-to-tail homo- and hetero-dimerizations.\textsuperscript{[19]}

![Scheme 2.5 Dimerization of vinyl amides](image)

The alkene head-to-tail homo-and hetero-dimerization may take place by an initial gold(I) activation of the alkene, followed by an attack of the second alkene-unit at the vinylic gold(I)-complex. By a cationic mechanism and through C-C double-bond activation, the reaction proceeds. A protodeauration by a 1,3-proton shift would enable regeneration of the vinylic C=C double bond together with the gold(I) catalyst, see Scheme 2.6. Due to the bulkyness of the substituents, the trans isomer would be the expected product from this mechanism.
However, recent publications suggest a different mechanism through an acid-catalyzed reaction. These studies indicate the formation of superacid HSbF$_6$ when phenylacetylene is reacted with gold(I) catalyst I, see Scheme 2.7, forming a digold complex. In this complex, gold replaces the terminal proton of phenylacetylene, generating the superacid HSbF$_6$. This superacid may be the active catalyst in the dimerization reactions.

Scheme 2.7 Formation of digold complex from gold(I) catalyst and phenylacetylene

### 2.5 Preparation of acetals

We wanted to study the gold(I) catalyzed cyclization reactions of vinylic enamides with propargyl acetals. These acetals could be synthesized from propargyl alcohol and vinyl ethers, as shown in Scheme 2.8.

Scheme 2.8 Preparation of propargyl acetals

A number of acetal protecting groups are used to avoid unwanted reactions of alcohols. If the alcohol is chiral, like the propargyl alcohol, the result may be a mixture of two diastereomers of the acetal. Two diastereomers may complicate purification and/or characterization.
2. Theory

The most utilized protecting acetal is tetrahydropyanyl ether (THP), see Scheme 2.9.

![Scheme 2.9 Preparation of THP group]

The oxonium intermediate is similar to the oxonium ion in normal acetal-formation of carbonyl compounds.\[^6\] By utilizing 2-methoxy-2-propyl ethers (MOP ethers) the problem of diastereomers will be avoided. MOP ethers can be prepared by treating the alcohol with 2-methoxypropene in the presence of an acid, similar to the preparation of 1-ethoxyethyl ether, see Scheme 2.11.

![Scheme 2.11 Mechanism for preparing MOP ethers]

As shown in Scheme 2.10 and Scheme 2.11, these reactions are acid catalyzed. \textit{para-}Toluene sulfonic acid (PPTS) is commonly used as catalyst in these reactions. It is stable as a solid, and as strong an acid as sulfuric acid.\[^6\] In addition it is cheap and readily available, as it is a byproduct in the synthesis of saccharin.\[^6\]

![Figure 2.5 Structure of catalyst, PPTS]
2.6 Preparation of vinyl amides

Functionalized aromatic and heteroaromatic amines are key building blocks for the syntheses of pharmaceuticals, polymers, or materials. To recognize their vast importance, many synthetic methods for the formation of C-N bonds have emerged.\textsuperscript{[22]} Enamides are important synthetic intermediates and there are a number of protocols for preparing them.\textsuperscript{[22]} However, they suffer from either low yields or a lack of stereocontrol in the double bond geometry.\textsuperscript{[23]} Due to their synthetic utility, the preparation of enamides has received considerable attention over the past decade. The introduction of chelating ligands resulted in major improvements and dramatic softening of the reaction conditions compared with the original Goldberg’s procedure.\textsuperscript{[22]} Buchwald and co-workers studied this reaction extensively and developed an experimentally simple and inexpensive catalytic system based on the use of 1,2-diamine ligands and K$_2$CO$_3$ as base, as shown in Scheme 2.12. This system is highly effective also for secondary amides. The reactions tolerates a variety of functional groups, including many that are not compatible with palladium catalysis.\textsuperscript{[22]}

\begin{equation}
\begin{array}{c}
R^1\text{CON}^+\text{R}^2 + \text{Br} = \text{CuI} \\
\text{N,N'-dimethylethylenediamine} \\
\text{K}_2\text{CO}_3 \\
\end{array}
\end{equation}

Scheme 2.12 Copper mediated cross-coupling of vinyl halide and amide

The copper catalyst coordinates to the vinyl halide, activating it for nucleophillic attack by the amide. This produces acid, neutralized by the base in the reaction mixture, here K$_2$CO$_3$. A cross-coupling between the amide and vinyl halide gives vinyl amide as the product (Scheme 2.13).

\begin{equation}
\begin{array}{c}
\text{Cu}^+ \text{I} \\
\text{Br} \text{CuI} \\
\text{HBr} \\
\end{array}
\end{equation}

Scheme 2.13 Suggested mechanism for copper catalyzed coupling of vinyl halide and amide
2.7 Use of product and results

Gold catalysis is an expanding field. Complex molecules are synthesized in few steps with high selectivity. Compounds synthesized in gold catalyzed reactions may be used as building blocks in further syntheses of complex molecules. Studies on gold(I) complexes will give further information on how to improve selectivity of different reactions.

By gold(I) catalyzed [3+2] cycloadditions of propargyl acetals and vinyl amides, cyclopentene derivatives are easily obtained. Reaction conditions are mild, and the reactions are selective. Different homo- and heterodimers of vinyl amides may be obtained in few step by reactions of vinyl amide, gold(I) catalyst and phenylacetylene.
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Chapter 3

Results and Discussion

This chapter is divided into five sections. Preparation of starting materials, including new propargyl acetals and vinyl amides are presented in section 3.1. The results from gold catalyzed cyclopentenyl-lation are presented in section 3.2. This includes cyclopentenyl derivatives from reactions between the different propargyl acetals and vinyl amides. Gold catalyzed dimerization of vinyl amides are further presented in section 3.3; including homodimerization (section 3.3.1) of cyclic and acyclic vinyl amides and heterodimerization (section 3.3.2) of two different vinyl amides. An unexpected development occurred during these studies. As a result the behaviour of the gold(I) catalyst is discussed in section 3.4. Outlook and perspectives are discussed in section 3.5.

New products are characterized by NMR, MS and IR, as far as there was sufficient amount. The respective melting points have been measured for solids. New compounds have been structure elucidated by NMR. 

3.1 Synthesis of starting materials

3.1.1 Syntheses of acetals

Propargyl acetals 1a and 1b was synthesized by reacting propargyl alcohol 2 with the appropriate vinyl ether, as shown in Scheme 3.1. The mechanism and theory for preparation of propargyl acetals EE and MOP are discussed in Chapter 2.5.

The procedure for the preparation of acetals from non-terminal propargylic alcohol is known\(^{25}\),
but methoxy acetal 1a and ethoxy acetal 1b have not previously been reported. The acetals were isolated as clear (1a) and yellow (1b) oils with respective yields of 60% and 40%. Both compounds are highly unstable at room temperature and immediately decompose into the alcohol and to other unidentified byproducts. Some of the decomposed material has similar retention on flash column as the desired product. This made purification on silica column difficult and ultimately resulting in moderate isolated yields. The ethoxy acetal 1b was less stable than the methoxy analogue, acetal 1a, and might also decompose on the column, affording low isolated yield. NMR-shift values for acetal 1b are complex, indicating the formation of diastereomers (Figure 3.1).

![Figure 3.1 Diastereotopic protons of 1b](image)

The diastereotopic protons are not a problem for acetal 1a. As discussed in Chapter 2.3, this compound has no acetal stereogenic centre. The solution to the decomposition problem was to use the acetal in further synthesis immediately after preparation and isolation. Another solution was to store the compound at low temperature to slow down the decomposition. It is evident from TLC and GC that conversion of alcohol 2 was complete after 3 h.

Characterizations of propargyl acetals 1a and 1b are based on NMR spectroscopy, MS and IR. Chemical shifts are assigned from NMR (Appendix A-B), see Figure 3.2 and Figure 3.3.

![Figure 3.2 Structure and chemical shifts for methoxy acetal 1a](image)

![Figure 3.3 Structure and chemical shifts for ethoxy acetal 1b](image)
3. Results and Discussion

3.1.2 Syntheses of vinyl amides

Attempts to synthesize vinyl amide 4a-b through the known addition-elimination method were performed, shown in Scheme 3.2.[26]

\[
\begin{align*}
R^1\text{NH} & + \text{Br} & \text{K}_2\text{CO}_3, \text{CH}_3\text{CN} & \text{reflux, 24 h} & R^1\text{N} & \equiv & R^2 \\
6a: R^1=\text{Ac, } R^2=\text{Me} & 5 & 7 & 4a: R^1=\text{Ac, } R^2=\text{Me} \\
6b: R^1=\text{Ac, } R^2=\text{Ph} & & & 4b: R^1=\text{Ac, } R^2=\text{Ph}
\end{align*}
\]

Scheme 3.2 Attempt to synthesize vinylamide 4a-b

TLC and GC showed no evidence of conversion of the starting material. The reaction time was increased from 24 hours to 48 hours, and the base altered between K$_2$CO$_3$, LiCO$_3$ or CeCO$_3$, had no effect on the reaction.

A different procedure through copper catalyzed cross-coupling reaction improved the results. Vinyl amides 4a-b were synthesized from amides 6a-b and vinylbromide 8 (Scheme 3.3), as described in General procedure B. These compounds were isolated as white solids, and respective yields were 43% and 33%. Both compounds were synthesized from a known procedure.[23] Compound 4a is also commercially available from Sigma-Aldrich. For further use in the gold catalyzed reactions, the commercial compound was utilized.

\[
\begin{align*}
R^2 & \text{NH} & \text{Br} & \text{Cul}, \text{NH}_2\text{CH}_2\text{CH}_2\text{NH}_2, \text{K}_2\text{CO}_3 & \text{reflux, 16 h} & R^1\text{N} & \equiv & R^2 \\
6a: R^1=\text{Ac, } R^2=\text{Me} & 8 & 4a: R^1=\text{Ac, } R^2=\text{Me} \\
6b: R^1=\text{Ac, } R^2=\text{Ph} & & 4b: R^1=\text{Ac, } R^2=\text{Ph}
\end{align*}
\]

Scheme 3.3 Synthesis of vinyl amides 4a-b

N-vinyl valerolactam 9 and 3-vinylloxazolidin-2-one 11 are previously reported, and they were synthesized from δ-valerolactam (10) and oxazolidin-2-one (12), as described for vinyl amides 4a-b. The only difference being reaction time, as shown in Scheme 3.4 and Scheme 3.5.

\[
\begin{align*}
\text{O} & \text{NH} & \text{Br} & \text{Cul}, \text{NH}_2\text{CH}_2\text{CH}_2\text{NH}_2, \text{K}_2\text{CO}_3 & \text{reflux, 20 h} & \text{O} & \equiv & \text{N} \\
10 & 8 & 9
\end{align*}
\]

Scheme 3.4 Synthesis of vinyl amide 9
3. Results and Discussion

Scheme 3.5 Synthesis of vinyl amide 11

N-vinyl valerolactam 9 was isolated as a bright yellow solid in 43% yield after purification with flash chromatography. Pure 3-vinyl oxazolidin-2-one 11 was isolated as a brown liquid in 89% yield. The crude product was not further purified. Yields and $^1$H-NMR shifts for the prepared vinyl amides are in accordance with litterature.$^{[27]}$

3.2 Gold(I) catalyzed [3+2] cycloaddition

Gold(I) catalyst I has been used in all gold(I) catalyzed reactions.

![Figure 3.4](image)

Figure 3.4 (Acetonitrile)[(2-biphenyl)di-tert-butylphosphine]gold(I) hexafluoroantimonate

During the studies of gold(I) catalyzed olefin cyclopropanation reactions of different propargyl esters, gold(I) catalyzed [3+2] cycloaddition of the terminal propargyl ester (15) with electron-rich vinyl compounds (16a-b) were reported , as shown in Scheme 3.6.$^{[3]}$

![Scheme 3.6](image)

Scheme 3.6 Formation of cyclopentenyl esters

The mechanism for these types of reactions are discussed in Chapter 2.3.
To further investigate the possible gold(I) catalyzed [3+2]-cycloaddition pathway, the electronic and steric nature reactants were varied. Propargylic (1a-b) and vinylic (4a-b, 9 and 11) species were used. Different combinations of the propargyl acetals and vinyl amides were added to the gold catalyst, then stirred at room temperature for 15-60 minutes, see Scheme 3.7.

Scheme 3.7 Gold(I) catalyzed [3+2] cycloaddition

3.2.1 Gold(I) catalyzed [3+2] cycloaddition with acetal 1a

Reactions with methoxy acetal 1a and the heterocyclic vinyl amide 9 gave to major products, 17a and 18a. These products were relatively easy to separate from the minor products with flash chromatography. The products were isolated as brown oils, in respective yields of 22% and 51%. The reaction time was increased compared to reactions with less steric hindered vinyl group (e.g heterocyclic vinyl amide 11). GC and TLC indicated full conversion of substrate 1a in 60 minutes. The suggested mechanism for the formation of products 17a and 18a by [3+2] cycloaddition is presented in Chapter 2.3.

Scheme 3.8 Synthesis of cycloaddition-products 17a and 18a

Expected to be the initially formed product, as suggested in Scheme 2.4, Chapter 2.3, compound 17a is the minor product. Isomerization of the double bond of the cyclopentene ring takes place during the reaction, giving the additional product 18a. Compound 18a is the major product because the double bond is conjugated to the phenyl group and the effect of the EWG on the amide. The two isomers are characterized by NMR, IR and MS (Appendix F-G). Figure 3.5 and Figure 3.6 show chemical shifts for compound 17a and 18a. Stereochemistry for compound 17a have been determined by H-H NOE-experiments (Appendix F.6).
3. Results and Discussion

Reaction of methoxy acetal 1a and the heterocyclic vinyl amide 11 also gave two major products, compound 17b and 18b (Scheme 3.9). They were isolated as colorless (17b) and brown (18b) oils, with respective yields of 14% and 36%. The reaction was similar to the synthesis of products 17a and 18a.

![Figure 3.5 Structure, chemical shifts and NOE-connections for 17a](image)

![Figure 3.6 Structure, chemical shifts for 18a](image)

Scheme 3.9 Synthesis of cycloaddition-products 17b and 18b

The colour of the reaction mixture rapidly changed from yellow to dark brown after adding the reactants to the gold(I) catalyst. GC and TLC indicated full conversion of acetal 1a in 20 minutes.
at room temperature. The reaction was fast compared to the synthesis of compounds 17a and 18a. The two isomers were characterized by NMR, IR and MS (Appendix H-I). Figure 3.7 and Figure 3.8 show chemical shifts for products 17b and 18b. Stereochemistry for compound 17b have been determined by H-H NOE-experiments (Appendix H.6)

The gold(I) catalyzed reactions between heterocyclic vinyl amides 9,11 and methoxy acetal 1a gave the expected cyclopentenyl products. They were easily isolated and characterized. However, replacing the heterocyclic vinyl amides with the acyclic vinyl amides 4a and 4b, different results were obtained (Scheme 3.10). TLC indicated many spots, and GC gave no indication of formation of a cyclopentenylation product formed. There were no major products in the reaction, all products had similar retention on flash chromatography. $^1$H-NMR of the crude product and isolated fractions after the flash chromatography revealed none of the characteristic peaks for the cyclopentenyl ring.
3. Results and Discussion

3.2.2 Gold(I) catalyzed [3+2] cycloaddition with acetal 1b

As discussed in section 3.1, acetal 1b was highly unstable and decomposed readily. Reactions with ethoxy acetal 1b and vinyl amides in gold(I) catalyzed [3+2] cycloadditions were unsuccessful (Scheme 3.11).

![Scheme 3.11 Attempt to synthesize compound 20](image)

All reactions were monitored by TLC and GC and these showed a rapid and full conversion of acetal 1b. However, based on GC, there were no sign of conversion into cyclopentenyl products. Each reaction gave indications of 6-7 close spots on TLC, difficult to separate by flash chromatography. Acetal 1b has one methyl group while acetal 1a has two methyl groups. The different pathway for the two acetals may be due to this decreased bulkyness of ethoxy acetal 1b.

In addition to react acetal 1b with vinyl amides 4a-b, 9 and 11, an attempt to react acetal 1b with the commercially available cyclic vinyl amine 22 failed, Scheme 3.12. Both TLC and GC indicated no conversion of acetal 1b after stirring overnight at room temperature, nor after 1 hour reflux. It seems as if carbonyl moiety is essential for such reactions to take place.

![Scheme 3.12 Attempt to synthesize compound 21](image)

A study of gold-catalyzed cyclizations of 1,6-diynes investigates the difference of methyl-and ethyl-substituents on the diynes. The studies showed lower reactivity towards cyclization of the ethyl-substituted diynes compared to methyl-substituted. These studies involves a di-substituted alkyne, where steric hindrance from substituents may play a greater role than from our mono-substituted acetals. However the sterical hindrance should be taken into consideration for the decreased reactivity for our reactions. Another factor for the difference in reactivity between methoxy acetal 1a and ethoxy acetal 1b may be the different leaving group ability for the two acetals. Acetone will be leaving group for acetal 1a. This is a better leaving group than the acetaldehyde produced in
reactions with acetal 1b, thus increases the reactivity for acetal 1a, as can be seen from the first step of the reaction (Scheme 3.13).

![Scheme 3.13 First step of proposed cyclopentenylation mechanism](image)

The formation of cyclopentenyl products 17-18 may indicate that the electron releasing alkoxy group of the propargyl acetals are important for stabilizing the allylic gold(I) species, as discussed in Scheme 2.3, Chapter 2.3, to favour the [3+2] cycloaddition reactions. This is in contrast to the electron withdrawing substrates, such as propargyl esters, who would rather undergo cyclopropagation.

### 3.3 Dimerization of vinyl amides

During our studies of the gold(I) catalyzed cyclization reactions of propargyl esters, it was discovered that some of the vinyl amides would rather undergo a head-to-tail dimerization instead of cyclization. Tail-to-tail coupled products of alkenes from reductive coupling through metallacycle have been reported, as discussed in Chapter 2.4. However, there were no reports on gold(I) catalyzed head-to-tail coupling. It was desirable to investigate further the coupling pathways of different vinyl amides (Scheme 3.14), and the possible role of the gold(I) catalyst in these reactions.

![Scheme 3.14 Dimerization processes](image)

Experiments conducted with propargylic substrates and vinyl amides, but without gold(I) catalyst, gave no dimerization. Nor did reactions with gold(I) catalyst and vinyl amide, without propargylic substrate. This indicates that the propargyl compound is necessary for the reaction. Further investigation indicated that the triple bond system needed to be terminal in order for a reaction to take place. Phenylacetylene is readily available and doesn’t require special reaction conditions, so this was our choice of triple bond system in the dimerization reactions. Our studies of the possible pathways for dimerization reactions are discussed in this section.

#### 3.3.1 Homodimerization of vinylamides

Experiments on homodimerization of acyclic vinyl amides 4a-b and heterocyclic vinyl amides 9 and 11 were conducted as described in *General Method D*, Chapter 5. Phenylacetylene, 24, equivalent to the vinyl amide was used. Phenylacetylene and vinyl amide were added to the gold(I) catalyst
3. Results and Discussion

in DCM and refluxed until complete conversion of the vinyl amide. Reactions were monitored by TLC and GC.

Dimer product 23 was obtained in 79% yield, by reacting vinyl amide N-vinyl valerolactam 9 in the presence of phenylacetylene and gold(I) catalyst under reflux for 24 hours (Scheme 3.15).

\[
\text{N} + \text{Ph} \xrightarrow{\text{reflux, 24 h}} \text{DCM} \quad \text{9} \quad \text{24} \quad \text{23}
\]

Scheme 3.15 Synthesis of dimerization product 23

The dimer product 23 was isolated as the only major product by flash chromatography. The white solid was characterized by NMR and MS. The chemical shifts are assigned by NMR-spectroscopy (Appendix J). The high characteristic \textit{trans} coupling-constant \(J=15\) confirms that the \textit{trans}-isomer is selectively formed. Figure 3.9 show chemical shift for product 23 determined by NMR.

![Figure 3.9 Structure and chemical shifts for dimer 23](image)

The gold(I) catalyzed reaction of the second cyclic amide, 3-vinylloxazolidin-2-one 11, was similar to dimerization of vinyl amide 9, and gave a 72% yield of dimer 25. The reaction was monitored by GC and TLC and indicated complete conversion of vinyl amide 11 after 20 hours reflux, as shown in Scheme 3.16.

\[
\text{O} + \text{Ph} \xrightarrow{\text{reflux, 24 h}} \text{DCM} \quad \text{11} \quad \text{24} \quad \text{25}
\]

Scheme 3.16 Synthesis of dimerization product 25

There was only one major product from the reaction. This was readily purified and isolated by flash chromatography, as decribed in Chapter 5.4. The chemical shifts are assigned by NMR-spectroscopy (Appendix K). Figure 3.10 shows chemical shifts for dimer product 25.
3. Results and Discussion

Acyclic vinyl amide $4b$ reacted similar as heterocyclic vinyl amides $9$ and $11$ and yielded 63% dimer product $26$, as shown in Scheme 3.17.

There was one major product from the reaction, and product $26$ was isolated as a brown oil (63% yield). Spectroscopic data (NMR) of dimer $26$ was different than that of dimer $23$ and $25$. It is apparent from $^1$H-NMR (Appendix L.1) and HSQC (Appendix L.3) that one methyl group gives rise to two signals at $\delta=1.82$ (br) and $\delta=2.17$ (s). It is known that for compounds of similar character, such as dimethylformamide (DMF), the two N-methyl groups give two different signals in $^1$H-NMR.\[28] These two peaks coalesce into one broad peak at $100^\circ C$ and one sharp peak at higher temperature. From this it is apparent that the two methyl groups are differently shielded at room temperature, whereas in higher temperature they become equivalent. The reason for this is well known and is due to a double bond character of the C-N bond, which results in a hindered rotation. Thus, the two methyl bonds are in different magnetic environment at room temperature. The barrier of rotation is overcome at higher temperature, of which the two methyl groups exchange places so rapidly, they are no longer distinguished by NMR. If we look at this effect for compound $26$, we can explain the two peaks corresponding to two different environments of one methyl group in $^1$H-NMR, see Scheme 3.18.

The reason why this effect is only apparent for one of the methyl groups in dimer $26$ may be because the double bond in the bridge between the two monomers is electron donating. Thus destabilizing a positive charge on the nitrogen closest, and therefore there will be no double bond character between this nitrogen and carbon.
Figure 3.11 shows the structure and chemical shifts for compound 26. The chemical shifts are assigned by NMR-spectroscopy of dimer 26 in CDCl$_3$ (Appendix L.1-L.5).

![Chemical structure and shifts for compound 26](image)

In general, the addition of D$_2$O to $^1$H-NMR samples enables the identification of -OH and -NH protons. In D$_2$O these protons are exchanged by deuterated proton and they disappear from the spectra.

$^1$H-NMR of dimer 26 in CDCl$_3$/D$_2$O revealed no proton exchange (Appendix L.8), confirming that the broad peaks at $\delta=1.82$ and $\delta=6.90$ are not exchangeable protons, such as -OH or -NH protons. However, $^1$H-NMR of dimer 26 in DMSO lead to a change in shift values for the methyl groups (Appendix L.7). This result is comparable to the change in shift values for DMF in CDCl$_3$ and DMSO, further indicating similar properties of the C-N bond for product 26.$^{[20]}$ The broad peak at $\delta=6.90$ in CDCl$_3$ appeared in DMSO as a splitted multiplet.

In contrast to reactions of acetyl phenyl substrate 4b, the acetyl methyl analouge 4a afforded more complex product mixtures. Vinyl amide 4a seems to be highly reactive in all reactions. In an attempt to synthesize a dimer of vinyl amide 4a, there were no major products. TLC and GC indicated several products, with similar retention on flash column.

At the end of this work, it was discovered by a Valencia research group, that phenylacetylene coordinates double to the gold(I) catalyst, where a $\sigma$-interaction between phenylacetylene and gold replaces the terminal proton, generating the superacid HSbF$_6$ of the counterion, as shown in Scheme 3.19.$^{[20]}$

![Scheme 3.19](image)

This acid formed in situ may be the active catalyst for the dimerization-reactions.
The total results of homodimerization obtained by this project and others are presented in Table 3.1.\textsuperscript{[30]}

<table>
<thead>
<tr>
<th>Amide number</th>
<th>Amide formation</th>
<th>Dimer yields(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>11</td>
<td>Yes</td>
<td>79</td>
</tr>
<tr>
<td>13</td>
<td>Yes</td>
<td>72</td>
</tr>
<tr>
<td>29*</td>
<td>Yes</td>
<td>85</td>
</tr>
<tr>
<td>30*</td>
<td>Yes</td>
<td>89</td>
</tr>
<tr>
<td>4a</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>4b</td>
<td>Yes</td>
<td>85</td>
</tr>
<tr>
<td>31*</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>32*</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>33*</td>
<td>No</td>
<td></td>
</tr>
</tbody>
</table>

*Work done by Post.Doc Naseem Iqbal\textsuperscript{[30]}

### 3.3.2 Heterodimerization of vinylamides

To continue the studies of dimerization, we wanted to investigate the potential for chemoselective heterodimerization between to different vinyl amides in the presence of gold(I) catalyst and phenylacetylene. Two vinyl amides with respectively electron withdrawing and electron releasing amide groups were chosen in order to obtain high selectivity of mixed dimer, see Scheme 3.20.

![Scheme 3.20](image)

Scheme 3.20 Attempt to synthesize heterodimer 34 from 11 and 31

The reaction between heterocyclic vinyl amide 11 and acyclic vinyl amide 31 gave only homodimer 25 (Scheme 3.16). However, corresponding reactions conducted by post.doc Naseem Iqbal yielded heterodimer 35 in 43% yield between electron deficient heterocyclic amide 29 and electron rich vinyl amide 31, see Scheme 3.21. This indicates that mixed dimerizations of vinyl amides are possible and should be investigated further.
3. Results and Discussion

3.4 Catalyst-studies

As described in section 3.3, a recently published article reports in situ formation of super acid HSbF$_6$ in the reactions with our gold(I) catalyst and phenylacetylene. The gold(I) catalyst coordinates to phenylacetylene to form an equilibrium, as described in Scheme 3.19, generating the superacid HSbF$_6$ (28) and a digold complex (27).

The generation of the super acid is the result of replacement of the terminal alkyne proton by a σ-interaction between carbon and gold. This is in contrast to previous assumptions that gold interacts with the π-cloud of the triple-bond systems. Research related to this work, using TFA as an acid catalyst, yielded a dimer without gold catalyst involved$^{[30]}$, but in poor yield and without complete conversion. This indicates that the acid may be the active catalyst in the dimerization reactions. HSbF$_6$ is a commercial available acid. Further studies will indicate if in situ generation of the super acid would be more convenient than adding the highly reactive super acid reactant. This would ultimately allow less harsh conditions.

3.5 Outlook and Perspectives

As a natural outlook for this work, further studies involving the gold catalyst and phenylacetylene should be conducted. The dimerization of vinyl amides were first discovered in gold(I) catalyzed reactions with propargyl acetics. It would be interesting to investigate if the propargyl acetics coordinate to gold, generating a digold complex similar to the one reported, and to see if it would be possible to isolate this complex. NMR and x-ray images of the complex would give information on this matter.

Further testing on reaction conditions regarding dimerization should also be conducted. It will be interesting to see if it would be possible to separately add the super acid as a reactant, or if it is better to generate this in situ from the gold catalyst and phenylacetylene. It will also be interesting to see the difference in reaction time, temperature, conversion, selectivity etc.

Regarding cycloaddition reactions, positive results are obtained from studies on other one-pot reactions being conducted in the research group. A suggestion on a one-pot reaction from alcohol 2 to cyclopentenyl products 17-18 is shown in Scheme 3.22.
Scheme 3.22 One-pot reaction from alcohol 2 to cyclic products 17-18
3. Results and Discussion
Chapter 4

Conclusion

In acid catalyzed reactions, two new propargyl acetals 1a-b (60% and 40% yield), has been synthesized from propargyl alcohol 2 and vinyl ethers 3a-b.

Four different vinyl amides were synthesized by copper catalyzed cross-coupling reactions. Vinyl amides 4a-b (33-43%) were obtained from amides 6a-b. N-vinyl valerolactam 9 was synthesized from δ-valerolactam 10 in 43% yield and N-vinylloxazolidin-2-one 11 was synthesized from oxazolidin-2-one 12 in 89% yield.

Gold(I) catalyst I was added to methoxy acetal 1a and heterocyclic vinyl amide 9 in DCM. The reaction gave [3+2] cycloaddition products 17a and 18a in 22% and 51% yield. Similarly, reaction between methoxy acetal 1a and N-vinylloxazolidin-2-one 11 gave cyclopentenyl products 17b and 18b in 14% and 36% yield. No [3+2] cycloaddition took place in reactions between methoxy acetal 1a and acyclic vinyl amides 4a-b, nor between ethoxy acetal 1b and the vinyl amides.

In the presence of gold(I) catalyst and phenylacetylene, vinyl amides 4b, 9 and 11 gave the corresponding homodimerization trans products 23 (79%), 25 (72%) and 26 (63%). Acyclic vinyl amide 4a yielded no dimer.

Heterodimerization reaction of electron withdrawing vinyl amide 11 and electron releasing vinyl amide 31 was unsuccessful. However, heterodimerization reaction of comparable compound 29 and 31 has been performed in the research group, and gave heterodimer 35 (43%).
Chapter 5

Experimental section

5.1 General

$^1$H-, $^{13}$C-, COSY-, HMBC-, -NOESY and HSQC-spektra were recorded on Bruker Avance DPX 300 MHz or 400 MHz spectrometer. All chemical shifts are reported in ppm (parts per million, $\delta$) referenced downfield to TMS ($\delta=0.0$). Coupling constants ($J$) are reported in Hertz (Hz) and all multiplicities are indicated as br (broadened), s (singlet), d (doublet), dd (doublet of doublets) t (triplet), dt (doublet of triplets), ddt (doublet of doublet of triplets), quin (quintet), m (multiplet) and dm (doublet of multiplets). COSY, HMBC, HSQC and NOESY experiments have been used to determine chemical shifts and structures (Appendix A-L).

Infrared spectra (IR) were recorded on Nicolet 20SX FT-IR spectrometer.

Accurate mass determination, EI and ESI, was performed on MAT95XL ThermoFinnigan and Agilent G1969 TOF MS instruments respectively. For ESI analyses, samples were injected into the instrument using an Agilent 1100 series HPLC. A direct injection analysis without any chromatography was performed for the EI analyses.

Reactions were monitored by gas chromatography (GC) performed on a Varian CP-3800. Thin layer chromatography (TLC) were performed on Merck TLC aluminum sheets, Silica gel 60 F$_{254}$. The TLC plates were visualized in either UV-lys (254 nm) or stained with p-anis aldehyde stain solution (5 mL conc. H$_2$SO$_4$, 1.5 mL absolute acetic acid and 3.7 mL p-anisaldehyde in 137 mL absolute ethanol) followed by heating. Flash column chromatography was performed using Supelco VersaFlash system with VersaFlash cartridges packed with 20-45 or 45-75 $\mu$m spherical silica based porous (70 Å) particles. All chemicals and solvents were of synthetic grade and were not further purified before use. All dry dichloromethane (DCM) was collected from a Braun MB SPS-800 purification system and stored over 4 Å molecular sieve nitrogen. All reactions were performed under a static atmosphere of nitrogen in dried glassware.
5. Experimental section

5.2 Preparation of starting materials

5.2.1 General procedure A: Preparation of acetal 1a-b

\[
\begin{align*}
\text{Ph} & \quad \text{\textod{2}} \\
\text{Ph} & \quad \text{\textod{1a}}: \text{R}^1=\text{Me}, \text{R}^2=\text{Me} \\
\text{Ph} & \quad \text{\textod{1b}}: \text{R}^1=\text{H}, \text{R}^2=\text{Et}
\end{align*}
\]

To a solution of 1-phenyl-2-propyn-1-ol in desired vinyl ether cooled to 0°C, a catalytic amount of PPTS was added. The reaction mixture was stirred at room temperature for 3 hours, until reaction was complete. The mixture was diluted with dichloromethane (120 mL) and washed with water (3*120 mL) and brine (120 mL). The organic layer was dried over MgSO₄ and the solvent was removed in vacuo to obtain the crude product. The residue was purified by silica gel VersaFlash in suitable eluent system to obtain the desired acetal.

Synthesis of \(1-(\text{2-Methoxypropan-2-yl})\text{oxy}\)prop-2-yn-1-yl)benzene (1a)

\[
\begin{align*}
\text{Ph} & \quad \text{O} \\
\text{OMe} & \quad \text{1a} \\
\text{OMe} & \quad \text{60\%}
\end{align*}
\]

Methoxy acetal 1a was synthesized according to General Procedure A from alcohol 2 (300.1 mg, 2.28 mmol) mixed with methoxypropene (18 mL) and PPTS (3 mg, catalytic amount) for 3 hr. Flash chromatography (n-pentane/EtOAc 50:1) yielded compound 1a (278.6 mg, 59.9%) as a clear liquid.

\(1a\): \(R_f=0.78\) (n-Pentane/EtOAc 4:1); \(\text{\textod{H-NMR}}\) (400 MHz, CDCl₃-TMS)(Appendix A.1): \(\delta\) 7.47 (d, 2H \text{arom}), 7.26-7.39 (m, 3H \text{arom}), 5.40 (d, \(J=2.3\) Hz, 1H, PhCH), 3.17 (s, 3H, OCH₃), 2.51 (d, \(J=2.3\) Hz, 1H, CH₃), 1.53 (s, 3H, CH₃);

\(\text{\textod{C-NMR}}\) (400 MHz, CDCl₃-TMS)(Appendix A.2): \(\delta\) 140.24 (1C, \text{C aromatic}), 128.70 (1C, \text{C aromatic}), 128.53 (1C, \text{C aromatic}), 127.98 (1C, \text{C aromatic}), 126.86 (1C, \text{C aromatic}), 126.60 (1C, \text{C aromatic}), 101.87 (1C, \text{C aromatic}), 84.47 (1C, \text{C aromatic}), 73.70 (1C, \text{C aromatic}), 62.60 (1C, \text{C aromatic}), 49.51 (1C, \text{OCH₃}), 25.41 (1C, \text{OCH₃}), 24.95 (1C, \text{OCH₃});

IR(thin film, \text{cm}^{-1})(\text{Appendix A.3}): 3286, 2990, 2831, 1256, 1146, 1067, 697;

HRMS (ESI) was performed for \(\text{C}_{13}\text{H}_{16}\text{O}_2\) [M-Na]⁺ but results were inconclusive due to decomposition.
5. Experimental section

Synthesis of (1-(1-Ethoxyethoxy)prop-2-yn-1-yl)benzene (1b)

Ethoxy acetal 1b was synthesized according to General Procedure A from alcohol 2 (500.2 mg, 3.79 mmol) mixed with ethylvinyld ether (24 mL) and PPTS (11 mg, catalytic amount). Compound 1b was isolated as a bright yellow liquid in 40.0% yield by flash chromatography (n-pentane/EtOAc 50:1).

1b: Rf = 0.78 (n-Pentane/EtOAc 4:1); 1H-NMR (400 MHz, CDCl3-TMS) (Appendix B.1): 7.51-7.59 (m, 2H arom), 7.34-7.40 (m, 3H arom), 5.45-5.46 (d, J=2.2 Hz, 0.5H, CHCH2), 5.34-5.35 (d, J=2.2 Hz, 0.5H, CHCCCH), 5.14-5.18 (q, J=5.4 Hz, 0.5H, OCH), 4.79-4.83 (q, J=5.4 Hz, 0.5H, OCH), 3.49-3.73 (m, 2H, CH2), 2.62-2.69 (d, J=2.24 Hz, 1H, CCHH), 1.40-1.42 (t, 3H, CHC), 1.21-1.27 (m, 3H, CH2CH3);

13C-NMR (400 MHz, CDCl3-TMS) (Appendix B.2): 138.73 (1C, C arom), 138.52 (1C, CCH), 128.61 (1C, C arom), 128.53 (2C, C arom), 128.40 (1C, C arom), 127.30 (1C, C arom), 98.28+97.85 (1C, OCH), 81.87+75.15 (1C, C arom CH), 66.79+66.35 (1C, CCHCH), 59.97+60.63 (1C, CH2), 20.11+20.03 (1C, OCH3), 15.38 (1C, CH2CH3);

IR (thin film, cm−1) (Appendix B.6): 3288, 2977, 2934, 1450, 1273, 1078, 1067, 697;

HRMS (ESI) was performed for C13H16O2 [M-Na]+ but results were inconclusive due to decomposition.

5.2.2 General procedure B: Preparation of vinyl amides 4b, 9 and 11

Under complete inert conditions, the amide, vinyl bromide (1.0 M soln in THF, 2.0 equiv), CuI (0.05 equiv), N,N’-dimethylethylenediamine (0.10 equiv) and K2CO3 (2.0 equiv) was added to a schlenk flask, fitted with magnetic stir bar and reflux condenser. The vial was sealed tightly using parafilm, and the reaction mixture was heated to 110°C and let stir overnight. Upon completion of the reaction, the mixture was filtered through Celite™, rinsed with EtOAc and the solvent was removed in vacuo to obtain the crude product. The crude product was purified with silica gel Versa Flash, using suitable eluent system of EtOAc in n-pentane, to obtain the desired enamide.
Synthesis of *N*-phenyl-*N*-methyl acetamide (4b)

Enamide 4b was synthesized according to General Procedure B from amide 6b (300.2 mg, 2.22 mmol) mixed with vinylbromide (4.43 mL 1M solution in THF, 4.43 mmol, 2 equiv), *N*,*N*-dimethyl ethylenediamine (23.2 mg, 0.263 mmol, 0.10 equiv), CuI (21.13 mg, 0.1109 mmol, 0.05 equiv) and K$_2$CO$_3$ (615 mg, 4.44 mmol, 2.0 equiv). Reaction was stirred at 110°C overnight and enamide 4b was isolated as white solid in 32.5% yield by flash chromatography (n-pentane/EtOAc 20:1).

4b: R$_f$=0.61(n-Pentane/EtOAc 4:1); $^1$H-NMR(400 MHz, CDCl$_3$-TMS)(Appendix C.1): δ 7.70 (m, 1H, NC$_H$), 7.43-7.52 (m, 3H, H$_{arom}$), 7.18-7.20 (d, 1H, C$_{H_2}$), 4.38-4.40 (d, 1H, $J$=9, C$_{H_2}$), 3.84-3.88 (d, 1H, $J$=16, C$_{H_2}$), 1.88 (s, 3H, C$_{H_3}$);

$^{13}$C-NMR(400 MHz, CDCl$_3$-TMS)(Appendix C.2): δ 166.80 (1C, C=O), 139.20 (1C, N$_C$H), 133.73 (1C, C$_{arom}$), 129.99 (2C, C$_{H_2}H_{arom}$), 128.92 (2C, C$_{H_2}H_{arom}$), 127.69 (1C, C$_{H_2}H_{arom}$), 96.27 (1C, C$_{CH_2}$), 23.27 (1C, C$_{H_3}$); $^1$H-NMR shifts and yields are according to literature.\cite{27}

Synthesis of *N*-Vinyl valerolactam (9)

Enamide 9 was synthesized according to General Procedure B from amide 10 (217.1 mg, 2.19 mmol) mixed with vinylbromide (4.43 mL 1M solution in THF, 4.43 mmol, 2 equiv), *N*,*N*-dimethyl ethylenediamine (34.1 mg, 0.386 mmol, 0.10 equiv), CuI (21.3 mg, 0.1118 mmol, 0.05 equiv) and K$_2$CO$_3$ (613 mg, 4.43 mmol, 2.0 equiv). The reaction was stirred at 110°C overnight and enamide 9 was isolated as bright yellow solid (117.7 mg, 43.0%) by flash chromatography (n-pentane/EtOAc 20:1).

9: R$_f$=0.42 (n-Pentane/EtOAc 4:1); $^1$H-NMR(400 MHz, CDCl$_3$-TMS)(Appendix D.1): δ 7.60-7.68 (dd, $J_1$=9.1 Hz, $J_2$=14.2 Hz, 1H, NCH), 4.42-4.49 (dd, $J_1$=16.3 Hz, $J_2$=20.1 Hz, 2H, CH$_2$CH$_2$), 3.40-3.43 (t, 2H, NCH$_2$), 2.50-2.53 (t, 2H, C=OCH$_2$), 1.82-1.94 (ddm, 4H, CH$_2$CH$_2$); $^{13}$C-NMR(400 MHz, CDCl$_3$-TMS)(Appendix D.2): δ 168.66 (1C, C=O), 132.44 (1C, NCH), 93.44 (1C, CH$_2$CH$_2$), 44.28 (1C, NCH$_2$), 32.94 (1C, C=OCH$_2$), 22.52 (1C, CH$_2$CH$_2$), 20.57 (1C, CH$_2$CH$_2$); $^1$H-NMR shifts and yields are according to literature.\cite{27}
5. Experimental section

Synthesis of 3-Vinyloxazolidin-2-one (11)

Enamide 11 was synthesized according to General Procedure B from amide 12 (221.2 mg, 2.54 mmol), vinylbromide (4.58 mL 1M solution in THF, 4.58 mmol, 2 equiv), N,N’-dimethylethylenediamine (32.5 mg, 0.368 mmol, 0.10 equiv), CuI (21.8 mg, 0.1145 mmol, 0.05 equiv) and K$_2$CO$_3$ (677 mg, 4.89 mmol, 2.0 equiv). Reaction was stirred at 110$^\circ$C overnight and compound 11 was obtained as dark oil (254.7 mg, 89.0%).

11: $^1$H-NMR (400 MHz, CDCl$_3$-TMS) (Appendix E.1): $\delta$ 6.84-6.90 (dd, $J_1$=8.9 Hz, $J_2$=15.8 Hz, 1H, NC$\text{H}$), 4.43-4.47 (t, $J$=7.9 Hz, 2H, OC$\text{H}$), 4.42-4.44 (d, $J$=15.8 Hz, 1H, CHC$\text{H}$), 4.28-4.32 (d, $J$=15.8 Hz, 1H, CHC$\text{H}$), 3.70-3.74 (t, $J$=8.2 Hz, 2H, NCH$_2$);

$^1$H-NMR shifts and yields are according to literature.$^{[27]}$

5.3 Gold(I) catalyzed [2+3] cycloaddition

5.3.1 General procedure C: Gold(I) catalyzed cyclization between acetal and vinyl amide

To a schlenk flask, the gold catalyst was added (0.05 equiv) and solved in DCM. The acetal (1.0 equiv) and enamide (3.0 equiv) was diluted with DCM and added simultaneously to the gold catalyst. The reaction mixture was stirred at room temperature for 15-60 min. Upon completion, the reaction mixture was quenched with NEt$_3$, filtered through Celite$^{TM}$, rinsed with DCM and the solvent was removed in vacuo to obtain the crude product. The crude product was purified with silica gel Versa Flash, using suitable eluent system of MeOH in DCM.
5. Experimental section

Synthesis of 1-(3-methoxy-2-phenylcyclopent-3-en-1-yl)piperidin-2-one (17a) and 1-(3-methoxy-2-phenylcyclopent-2-en-1-yl)piperidin-2-one (18a)

According to General Procedure C, methoxy acetal 1a (31.5 mg, 0.150 mmol) and vinyl amide 9 (65.2 mg, 0.520 mmol) were added to the gold catalyst (7.1 mg, 9.1 µmol) in DCM and stirred at room temperature for 60 minutes. Flash chromatography (DCM/MeOH 50:1) yielded compound 17a (8.91 mg, 22.0%) and 18a (21.4 mg, 51.0%) as dark yellow oils.

17a: Rf = 0.31 (50:1 DCM/MeOH); 1H-NMR (400 MHz, CDCl3-TMS)(Appendix F.1): δ 7.31-7.40 (m, 5H arom), 5.14 (dt, J=5.5 Hz, 1H, CHN), 4.69 (m, 1H, C=CH), 3.85-3.86 (d, J=4.6 Hz, 1H, C=OCH), 3.60 (s, 3H, OC6H5), 3.21-3.34 (dm, 2H, C=OCH2), 2.67-2.74 (ddt, J1=2.0 Hz, J2=8.5 Hz, J3=4.8 Hz, J4=6.2 Hz, 1H, CHCH2), 2.36-2.39 (t, J=6.5 Hz, 2H, NCH2), 1.81-1.86 (m, 2H, NCH2C6H5), 1.74-1.79 (m, 2H, CH2CH2);

13C-NMR (400 MHz, CDCl3-TMS)(Appendix F.2): δ 169.5 (1C, C=O), 159.6 (1C, CO), 141.3 (1C, C=OCH2), 128.6 (2C, CH2arom), 127.7 (2C, CH2arom), 126.7 (1C, CHarom), 94.0 (1C, C=CH), 60.1 (1C, CHN), 56.8 (1C, OCH3), 53.2 (1C, PhCH), 43.4 (1C, O=CHCH2), 32.7 (1C, CH2CH2), 31.2 (1C, NCH2), 23.4 (1C, O=CH2CH2), 21.0 (1C, NCH2CH2);

IR(thin film, cm⁻¹)(Appendix F.7): 2942, 2361, 1631, 1172, 696;

HRMS (EI) calcd for C17H21NO2 [M-H]+ 272.1645, obsd 272.1645;

18a: Rf = 0.23 (50:1 DCM/MeOH); 1H-NMR (400 MHz, CDCl3-TMS)(Appendix G.1): δ 7.53 (d, J=7.4 Hz, 2H arom), 7.28 (t, J=5.4 Hz, 2H arom), 7.12 (t, J=7.4 Hz, 2H arom), 6.28-6.30 (m, 1H, CHN), 3.79 (s, 3H, OCH3), 3.38-3.45 (m, 2H, C=OCH2), 3.12-3.14 (m, 2H, CH2CH2), 2.85-2.90 (m, 2H, NCH2), 2.35-2.40 (t, J1=7.2 Hz, J2=6.7 Hz, 2H, CHCH2CH2), 1.63-1.71 (m, 3H, NCH2, C=OCH2CH2), 1.43-1.47 (m, 2H, NCH2CH2);

13C-NMR (400 MHz, CDCl3-TMS)(Appendix G.2): δ 169.9 (1C, C=O), 157.7 (1C, CO), 134.2 (1C, C=OCH2), 128.1 (2C, CH2arom), 126.4 (2C, CH2arom), 125.6 (1C, CH2arom), 110.4 (1C, C=CH), 56.8 (1C, CHN), 56.6 (1C, OCH3), 41.0 (1C, C=OCH2), 32.5 (1C, CH2CH2CH2), 28.9 (1C, CH2CH2), 24.7 (1C, NCH2), 23.1 (1C, O=CH2CH2), 20.9 (1C, NCH2CH2);

IR(thin film, cm⁻¹)(Appendix G.7): 2942, 2362, 1622, 1442, 1165, 696;

HRMS (EI) calcd for C17H21NO2 [M-H]+ 272.1645, obsd 272.1645;
5. Experimental section

Synthesis of 3-(3-methoxy-2-phenylcyclopent-3-en-1-yl)oxazolidin-2-one (17b) and 3-(3-methoxy-2-phenylcyclopent-2-en-1-yl)oxazolidin-2-one (18b)

According to General Procedure C, methoxy acetal 1a (106.2 mg, 0.520 mmol) and vinyl amide 11 (171.3 mg, 1.51 mmol) were added to the gold catalyst (22.0 mg, 28.5 µmol) in DCM and stirred at room temperature for 20 minutes. Flash chromatography (DCM/MeOH 50:1) yielded compound 17b (19.3 mg, 14.0%) as a colourless oil and 18b (48.1 mg, 35.0%) as yellow oil.

17b: Rf = 0.65 (20:1 DCM/MeOH); 1H-NMR(400 MHz, CDCl3-TMS)(Appendix H.1): δ 7.19-7.35 (m, 5H arom), 4.72 (d, J = 1.4 Hz, 1H, C=CH), 4.40-4.45 (m, 1H, CHN), 4.32-4.37 (m, 2H, NCH2C2H), 3.77-3.78 (d, 1H, PhCH), 3.63 (s, 3H, OCH3), 3.56-3.62 (m, 2H, NCH2C2H), 2.76-2.83 (ddt, J1 = 2.2 Hz, J2 = 5.6 Hz, 1H, CHC2H), 2.32-2.38 (dm, J = 15.6 Hz, 1H, CHCH2), 1.74-1.79 (m, 2H, CH2C2H);

13C-NMR(400 MHz, CDCl3-TMS)(Appendix H.2): δ 159.6 (1C, C=O), 159.4 (1C, C=O), 139.9 (1C, C arom), 128.7 (2C, CH arom), 127.6 (2C, CH arom), 127.1 (1C, CH arom), 93.2 (1C, C=CH), 61.9 (1C, NCH2), 59.9 (1C, NCH), 56.8 (1C, OCH3), 54.1 (1C, PhC), 41.6 (1C, OCH2), 31.3 (1C, CH2C2H);

IR(thin film, cm⁻¹)(Appendix H.7): 2934, 1736, 1251, 1229, 700;

HRMS (ESI) (Appendix H.8) calcd for C15H17NO3 [M-Na]^+ 259.1208, obsd 259.1213;

18b: Rf = 0.33 (20:1 DCM/MeOH); 1H-NMR(400 MHz, CDCl3-TMS)(Appendix I.1): δ 7.60 (d, J = 7.4 Hz, 2H arom), 7.22 (t, J = 7.8 Hz, 2H arom), 7.16 (t, J = 7.4 Hz, 1H arom), 5.47-5.49 (t, J1 = 2.5 Hz, J2 = 6.1 Hz, 1H, CHN), 4.05-4.26 (dm, 2H, CHCH2CH2), 3.35 (s, 3H, OCH3), 3.37-3.43 (q, 1H, CHCH2CH2), 3.14-3.19 (q, 1H, CHCH2CH2), 2.68-2.85 (m, 2H, NCH2CH2), 2.39-2.48 (dq, 1H, NCH2CH2O), 1.80-1.88 (dq, 1H, NCH2CH2O);

13C-NMR(400 MHz, CDCl3-TMS)(Appendix I.2): δ 158.0 (1C, C=O), 157.9 (1C, CO), 133.8 (1C, C arom), 128.4 (2C, CH arom), 126.4 (2C, CH arom), 125.9 (1C, CH arom), 109.5 (1C, C=CH), 61.9 (1C, CH2), 57.5 (1C, CHN), 56.8 (1C, OCH3), 40.3 (1C, CHCH2), 28.7 (1C, NCH2CH2O), 25.1 (1C, NCH2CH2O);

IR(thin film, cm⁻¹)(Appendix I.3): 2944, 2355, 1731, 1240, 1164, 697;

HRMS (ESI) (Appendix I.8) calcd for C15H17NO3 [M-Na]^+ 259.1208, obsd 259.1212;
5.4 Dimerization

\[
\begin{align*}
\text{R}^1 & \text{N} \equiv \\
\text{R}^2 & + \text{Ph} \equiv \\
\text{N} \equiv
\end{align*}
\]

\[
\begin{array}{c}
\text{R}^1 \\
\text{R}^2 \\
\end{array}
\]

\[
\begin{array}{c}
\text{N} \\
\text{R}^2 \\
\end{array}
\]

\[
\begin{array}{c}
\text{N} \\
\text{R}^1 \\
\end{array}
\]

Scheme 5.4 Homodimerization

5.4.1 General procedure D: Dimerization of vinyl amide in presence of triplebond system

To a schlenk flask, the gold catalyst was added (0.05 equiv) and solved in DCM. Phenylacetylene (1.0 equiv) and enamide (1.0 equiv) was diluted with DCM and added simultaneously to the gold catalyst. The reaction mixture was stirred under reflux for 20-24 hours. Upon completion, the reaction mixture was quenched with \(\text{NEt}_3\), filtered through Celite\textsuperscript{TM}, rinsed with DCM and the solvent was removed \textit{in vacuo} to obtain the crude product. The crude product was purified with silica gel Versa Flash, using suitable eluent system of MeOH in DCM.

Synthesis of \((E)-1,1^-{(\text{but-1-ene-1,3-diyl)bis(piperidin-2-one (23}}

\[
\begin{align*}
\text{O} & \equiv \\
\text{N} & \\
\text{O} & \equiv
\end{align*}
\]

Dimer 23 was synthesized according to General Procedure D from vinyl amide 9 (54.6 mg, 0.436 mmol), phenylacetylene (51.6 mg, 0.506 mmol) and gold(I) catalyst (17.7 mg, 22.9 µmol) in DCM. Reaction mixture was stirred under reflux for 24 hours. Flash chromatography (DCM/MeOH 40:1) yielded dimer 23 (86.3 mg, 77.0%) as a white solid.

23: \(R_f= 0.24 \) (DCM/MeOH 20:1); \(^1\text{H}-\text{NMR}(400 \text{ MHz, CDCl}_3\text{-TMS})(\text{Appendix J.1}): \delta 7.48-7.52 \) (dd, \(J_1=1.44 \text{ Hz, } J_2=15.0, 1\text{H, NCH}) , 5.39-5.42 \) (m, \(1\text{H, CH=C}) , 4.99-5.05 \) (dd, \(J_1=5.6 \text{ Hz, } J_2=14.9 \text{ Hz, } 1\text{H, CH}_3Ch) , 3.36-3.39 \) (t, \(2\text{H, NCH}_2) , 3.12-3.14 \) (m, \(2\text{H, C=OCH}_2) , 2.46-2.50 \) (t, \(2\text{H, NCH}_2) , 2.38-2.41 \) (m, \(2\text{H, C=OCH}_2) , 1.78-1.92 \) (m, \(2\text{H, C=OCH}_2CH_2) , 1.69-1.74 \) (m, \(6\text{H, CH}_2CH_2CH_2, CH_2CH_3CH_2) , 1.27-1.29 \) (d, \(3\text{H, CH}_3) ;

\(^{13}\text{C}-\text{NMR}(400 \text{ MHz, CDCl}_3\text{-TMS})(\text{Appendix J.2}): 169.30 \) (1C, C=O) , 168.58 \) (1C, C=O) , 128.39 \) (1C, NCH=C) , 110.19 \) (1C, CH=CHCH) , 48.10 \) (1C, CH=CH) , 45.26 \) (1C, NCH_2) , 41.75 \) (1C, C=OCH_2) , 32.93 \) (1C, NCH_2) , 32.57 \) (1C, C=OCH_2) , 23.27 \) (1C, CH_2CH_2CH_2) , 22.60 \) (1C, C=OCH_2CH_2) , 21.08 \) (1C, CH_2CH_2CH_2) , 20.50 \) (1C, CH_2CH_2CH_2) , 16.33 \) (1C, CH_3) ;

HRMS (EI) calcd for \(C_{14}H_{22}N_2O_2 \) [M-H]^+ 250.1676, obsd 250.1676.
5. Experimental section

Synthesis of (E)-3,3’-(but-1-ene-1,3-diyl)bis(oxazolidin-2-one (25)

Dimer 25 was synthesized according to General Procedure D from vinyl amide 11 (113.4 mg, 1.00 mmol), phenylacetylene (92.8 mg, 0.909 mmol) and gold(I) catalyst (33.1 mg, 42.9 µmol) in DCM. Reaction mixture was stirred under reflux for 20 hours. Flash chromatography (DCM/MeOH 30:1) yielded dimer 25 (162.9 mg, 72.0%) as a light yellow solid.

\[
\text{25: } R_f = 0.65 \text{ (DCM/MeOH 20:1); } ^1\text{H-NMR}(400 MHz, CDCl}_3\text{-TMS)(Appendix K.1): } \delta 6.80-6.83 \text{ (d, } J=14.8 \text{ Hz, 1H, NC=CH)}, 4.85-4.90 \text{ (dd, } J_1=5.9 \text{ Hz, } J_2=8.6 \text{ Hz, 1H, CH}_2\text{CHCH}), 4.54-4.61 \text{ (quint, } J=6.6, 1H, NCH), 4.44-4.51 \text{ (t, } J=7.8 \text{ Hz, 2H, OCH}_2), 3.48-3.72 \text{ (t, } J=8.2 \text{ Hz, 2H, NCH}_2), 1.35-1.36 \text{ (d, } J=7.0 \text{ Hz, 3H, CH}_3); \\
\]

\[
\text{IR(neat, cm}^{-1}\text{)(Appendix K.7): } 3293, 2923, 1731, 1480, 1230, 697; \\
\text{HRMS (EI) calcd for C}_{10}H_{14}N_2O_4 \text{ [M-H]}^+ 226.0948, \text{ obsd 226.0949.}
\]

Synthesis of (E)-N,N’-(but-1-ene-1,3-diyl)bis(N-phenylacetamide) (26)

Compound 26 was synthesized according to General Procedure D from vinyl amide 4b (77.1 mg, 0.480 mmol), phenylacetylene (51.3 mg, 0.503 mmol) and gold(I) catalyst (19.2 mg, 24.8 µmol) in DCM. Reaction mixture was stirred under reflux for 2 hours. Flash chromatography (DCM/MeOH 30:1) yielded compound 26 (108.8 mg, 63.7%) as a yellow oil.

\[
\text{26: } R_f = 0.13 \text{ (DCM/MeOH 20:1); } ^1\text{H-NMR}(400 MHz, CDCl}_3\text{-TMS)(Appendix L.1): } \delta 7.45-7.54 \text{ (m, 4H$_{arom}$), 7.28-7.35 \text{ (m, 4H$_{arom}$), 7.04 (d, } J=5.8 \text{ Hz, 2H$_{arom}$), 6.90 (br, 1H, CH=CHN), 5.47-5.52 \text{ (quin, } J=6.8 \text{ Hz, 1H, NCH), 4.25-4.30 (dd, } J_1=6.7 \text{ Hz, } J_2=14.5 \text{ Hz, 1H, NCH=CH), 2.17 (s, 1H, O=CCH$_3$), 1.82 (br, 3H, O=CCCH$_3$), 1.69 (s, 3H, C=OCH$_3$), 1.16-1.18 (d, } J=6.8 \text{ Hz, 3H, NCHCH$_3$); \\
\]

\[
\text{1H-NMR(400 MHz, DMSO)(Appendix L.7): } \delta 7.35-7.56 \text{ (m, 8H$_{arom}$), 7.20-7.27 \text{ (m, 2H$_{arom}$), 6.99-7.02 (m, 1H, CH=CHN), 5.21-5.34 (quin, } J=7.1 \text{ Hz, 1H, NCH), 4.03-4.08 (dd, } J_1=7.6 \text{ Hz, } J_2=14.4
\]
5. Experimental section

Hz, 1H, NCH=CH), 2.03 (s, 1H, O=CCH₃), 1.74 (br, 3H, O=CCH₃), 1.60 (s, 3H, C=OC₃H₃), 1.00-1.02 (d, J=6.8 Hz, 3H, NCHCH₃);

¹³C-NMR(400 MHz, CDCl₃-TMS)(Appendix L.2): 169.65 (1C, C=O), 168.68 (1C, C=O), 139.34 (1C, C_{arom}), 130.15 (1C, C_{arom}), 129.99 (1C, C_{H_{arom}}), 129.01 (2C, C_{H_{arom}}), 128.91 (2C, C_{H_{arom}}), 128.73 (2C, C_{H_{arom}}), 128.13 (2C, C_{H_{arom}}), 124.06 (1C, C_{H_{arom}}) 119.81 (1C, NCH), 114.31 (1C, NCH=CH), 49.80 (1C, CH₃CH), 24.54 (1C, C=OC₃H₃), 23.30 (1C, C=OC₃H₃), 18.25 (1C, CHCH₃);

IR(thin film, cm⁻¹)(Appendix L.6): 3293, 3064, 2973, 2359, 1656, 1260, 957;
Due to technical problems HRMS could not be performed for compound 26.
Bibliography


Appendix A

Methoxy acetal 1a

A.1 $^1$H-NMR Methoxy acetal 1a
A.3 IR Methoxy acetal 1a
Appendix B

Ethoxy acetal 1b

$^1$H-NMR Ethoxy acetal 1b
**B. Ethoxy acetal**

**13C-NMR Ethoxy acetal 1b**

---

**F2 - Acquisition Parameters**
- Data: 20120202
- Time: 3.30
- INSTRUM: spect
- PRMHD: 5 mm FA02, JRC
- CPMG: 200-900
- TD: 65.336
- SOLVENT: CDCl3
- NS: 512
- DD: 4
- SMR: 23980.814 Hz
- FIDRES: 0.365918 Hz
- AQ: 1.3664756 sec
- BG: 228.1
- DM: 20,850 usec
- DE: 6.00 usec
- TE: 297.0 K
- D1: 2.00000000 sec
- d13: 0.03000000 sec
- DELTA: 1.8999998 sec
- T0: 1

**---- CHANNEL f1 ----**
- MAX1: 1.3C
- F1: 6.50 usec
- F12: -4.00 dB
- SF21: 100.6228298 MHz

**---- CHANNEL f2 ----**
- CPDO22: waltz16
- MAC2: 1H
- PCDO22: 95.00 usec
- PL2: -4.00 dB
- PL12: 10.12 dB
- PL13: 18.15 dB
- SF22: 400.1316005 MHz

**F2 - Processing parameters**
- Z1: 32768
- SF: 100.6127690 MHz
- NCM: 512
- SSB: 0
- MB: 0 Hz
- GB: 0
- PC: 1.40
Current Data Parameters
NAME MK015-02a
PROCNO 1
EXPNO 6

F2 - Acquisition Parameters
Data_ 20120202
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INSTRUM spect
PROBND 5 mm PAOL 13C
POLPROG dept135
TD 65356
SOLVENT CDCl3
NS 512
DS 4
SNR 23960.81 Hz
PIONE 0.166618 Hz
AQ 1.366476 sec
DM 15004
DE 20.850 usec
DE 6.00 usec
DELTA 0.00000828 sec
d12 0.0000200 sec
d2 0.00344828 sec
DELTA 0.0000828 sec

======== CHANNEL f1 ========
SFO1 100.6228298 MHz
PL1 6.00 usec
p2 13.00 usec
P1 6.50 usec
NUC1 13C

======== CHANNEL f2 ========
SFO2 400.1316005 MHz
PL12 −6.00 dB
PL2 13.13 dB
p4 21.00 usec
PCPD2 95.00 usec
P3 10.50 usec
NUC2 1H
CPDPRG waltz16

F2 - Processing parameters
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SF 100.6127690 MHz
CMW 0
SSB 0
LB 0 Hz
GR 0
PC 1.40
B. Ethoxy acetal 1b

B.3 HSQC-NMR Ethoxy acetal 1b
B.4 COSY-NMR Ethoxy acetal 1b
B.5 HMBC-NMR Ethoxy acetal 1b
B.6 IR Ethoxy acetal 1b
Appendix C

Vinyl amide 4b

C.1 $^1$H-NMR Vinyl amide 4b
C. Vinyl amide

13C-NMR Vinyl amide 4b

Current Data Parameters
NAME GB013
PROCNO 1

F2 - Acquisition Parameters
Date 2011/03
Time 22:19
INSTRM nmr-spect
PULPROG zgpg30
ROD 1 mm POL 13C
T1 655.36
SOLVENT CDCl3
NS 256
DS 4
SNR 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3644756 sec
RG 90.5
DM 20.850 usec
DE 6.00 usec
TE 300.0 K
D1 0.0000000 sec
d1l 0.0000000 sec
DELTA 1.8999998 sec
T00 1

---------- CHANNEL f1 ----------
NUC1 13C
F1 6.50 usec
PL1 -6.00 dB
SFO1 100.6228298 MHz

---------- CHANNEL f2 ----------
NUC2 1H
P12 5.00 usec
PL2 -6.00 dB
P12 13.13 usec
PL3 13.13 dB
SFO2 400.1316005 MHz

F2 - Processing parameters
SI 32768
CF 100.6127650 MHz
MOD EM
SUS 0
LB 3.00 Hz
GB 0
FC 1.40
C. Vinyl amide 4b
Appendix D

N-vinyl valerolactam 9

D.1 $^1$H-NMR N-vinyl valerolactam 9
Current Data Parameters
NAME            GB011
EXPNO            2
PROCNO            1

F2 – Acquisition Parameters
Date-            20110929
Time-            17:49
INSTUM          spect
FIDRES          0.365918 Hz
AQ             1.366476 sec
DG             20.850 usec
TE              297.0 K
D1             2.00000000 sec
d11            0.03000000 sec
DELTA         1.89999998 sec
TOO            1

----- CHANNEL f1 ----- 
NUC1          13C
F1            6.50 usec
PL1          -6.00 dB
SFO1       100.628298 MHz

----- CHANNEL f2 ----- 
CPDPRG2      waltz16
NUC2          1H
F20            95.00 usec
PL2           -6.00 dB
PL12         13.13 dB
PL13          18.50 dB
SFO2     400.1316005 MHz

F2 – Processing parameters
S1            32768
SF          100.6127690 MHz
COM            0
SSB            0
LB             2.00 Hz
GB            0
PC          1.40
D. N-vinyl valerolactam 9
Appendix E

3-vinylloxazolidin-2-on 11

E.1 $^1$H-NMR 3-vinylloxazolidin-2-on 11
Appendix F

[3+2] cycloaddition product 17a

F.1 $^1$H-NMR [3+2] cycloaddition product 17a
F.3 HSQC-NMR [3+2] cycloaddition product 17a
F.4 COSY-NMR [3+2] cycloaddition product 17a
F.5  HMBC-NMR [3+2] cycloaddition product 17a
F.7  IR [3+2] cycloaddition product 17a
Appendix G

[3+2] cycloaddition product 18a

G.1 $^1$H-NMR [3+2] cycloaddition product 18a
G.3 HSQC-NMR [3+2] cycloaddition product 18a
G.4 COSY-NMR [3+2] cycloaddition product 18a
G.5 HMBC-NMR [3+2] cycloaddition product 18a
G.6 NOESY-NMR [3+2] cycloaddition product 18a
G.7 IR [3+2] cycloaddition product 18a
Appendix H

[3+2] cycloaddition product 17b

H.1 $^1$H-NMR [3+2] cycloaddition product 17b
H. [3+2] cycloaddition product 17b

H.3 HSQC-NMR [3+2] cycloaddition product 17b
H.4 COSY-NMR [3+2] cycloaddition product 17b
H.5  HMBC-NMR [3+2] cycloaddition product 17b
H.6 NOESY-NMR [3+2] cycloaddition product 17b
H.7 IR [3+2] cycloaddition product 17b
H.8 MS [3+2] cycloaddition product 17b
H. [3+2] cycloaddition product 17b
Appendix I

[3+2] cycloaddition product 18b

I.1 $^1$H-NMR [3+2] cycloaddition product 18b
I. 

[3+2] cycloaddition product 18b

C-NMR [3+2] cycloaddition product 18b

ppm

25.14
28.77
40.31
56.75
56.82
57.47
61.90
109.46
125.90
125.99
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128.58
133.84
157.93
158.04

PC                 1.40
GB       0
LB       0 Hz
SSB      0
WDW                  no
SF          100.6127690 MHz
SI                32768

F2 − Processing parameters
SFO2        400.1316005 MHz
PL13              18.50 dB
PL12              13.13 dB
PL2               −6.00 dB
PCPD2             95.00 usec
NUC2                 1H
CPDPRG2         waltz16
======== CHANNEL f2 ========
SFO1        100.6228298 MHz
PL1               −6.00 dB
P1                 6.50 use
NUC1                13C
======== CHANNEL f1 ========
TD0                   1
DELTA        1.89999998 sec
d11          0.03000000 sec
D1           2.00000000 sec
TE                297.0 K
DELTA         1.89999998 sec
T00                  1

====== CHANNEL f1 ======
M11                 13C
P1               6.50 use
P2                −6.00 dB
SFO1           100.6228298 MHz

====== CHANNEL f2 ======
CPDPRG2         waltz16
M22                 1H
PCPD2              99.00 use
P22                −6.00 dB
P12                10.13 dB
P22                18.15 dB
SFO2            400.1316005 MHz

F2 − Processing parameters
D1            32.768
GR      100.6127690 MHz
MCM                  0
SSB                 0
LB                 0 Hz
GB                 0
PC                 1.40
I.3 HSQC-NMR [3+2] cycloaddition product 18b
I.4 COSY-NMR [3+2] cycloaddition product 18b
I.5 HMBC-NMR [3+2] cycloaddition product 18b

I.5.1 HMBC-NMR spectrum of [3+2] cycloaddition product 18b
I.6 NOESY-NMR [3+2] cycloaddition product 18b
I.7 IR [3+2] cycloaddition product 18b
I.8 MS [3+2] cycloaddition product 18b

Qualitative Compound Report

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DA Method: ExtractForMPP_KFD.m

Comment: Sample information is unavailable.
I. $[3+2]$ cycloaddition product $18b$
Appendix J

Dimerization product 23

J.1 \(^1\)H-NMR Dimerization product 23
J. 3  HSQC-NMR Dimerization product 23
Appendix K

Dimerization product 25

K.1 $^1$H-NMR Dimerization product 25
K.3 HSQC-NMR Dimerization product 25
K.5 HMBC-NMR Dimerization product 25
K.6 NOESY-NMR Dimerization product 25
K.7 IR Dimerization product 25
Appendix L

Dimerization product 26

L.1 $^1$H-NMR Dimerization product 26
L.3 HSQC-NMR Dimerization product 26
L.4  COSY-NMR Dimerization product 26
L.5  HMBC-NMR Dimerization product 26
L.6   IR Dimerization product 26
L.7  
1H-NMR: Dimerization product 26 in DMSO
L.8 $^1$H-NMR Dimerization product 26 in CDCl$_3$/D$_2$O